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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/739,882	12/18/2003	Zhendong Jin	875.080US1	9688

21186 7590 08/05/2005

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EXAMINER	
COVINGTON, RAYMOND K	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/739,882	JIN ET AL.	
	Examiner	Art Unit	
	Raymond Covington	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 18-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14-16* is/are allowed.

6)☒ Claim(s) *1-13 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

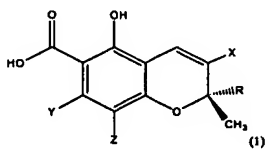
The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the method of preparing compounds of the formula



(I)

Wherein R, X, Y and Z are organic Substituents that do not interfere with The condensation of formula (2).

The state of the prior art: The state of the prior art is that it involves determining which compounds do not interfere with the condensation of (2) and applying them to the claimed process.

The predictability in the art: The process requires every organic substituent to be individually assessed and is thus unpredictable. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

The presence or absence of working examples:

There are insufficient exemplifications to support the use of all known organic substituents in the claimed process. The specification on pages 9 and 10 disclose a very limited working example. Page 6 of the specification lists only substituents where X, Y and Z include (C_1-C_2) alkyl, preferably (C_1-C_4) alkyl, (C_8-C_{10}) aryl, alkylaryl, aralkyl, alkaralkyl, wherein the alkyl groups optionally comprise 1 -3 double bonds, and can be interrupted by 1-2 O or N(C_1-C_4) alkyl R can have the same definition and is preferably a terpenoid group.

The amount of direction or guidance present: The specification on pages 10-11 provides very little guidance on how to make compounds within the full scope of the recited claims.

The breadth of the claims: The claims are drawn a method of preparing compounds wherein R, X, Y and Z are organic substituents that do not interfere with The condensation of formula (2).

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine which organic substituents that do not interfere with the condensation of formula (2) out of all such known organic substituents.

The level of the skill in the art: The level of skill in the art is high. Each embodiment of the invention is required to be individually assessed to determine which compounds exhibit the desired activity in the process.

Thus, the specification fails to provide sufficient support of the broad method recited in applicants' claims. As a result necessitating one of ordinary skill to perform an exhaustive search in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which organic substituents would work, with no assurance of success.

Claims 2-13 are rejected too the extent they depend on a rejected base claim.

Claims 5 and 6 recite the limitation "$N[(C_2\text{-}C_4)alkyl]_3$ is Net_3" or "$N[(C_2\text{-}C_4)alkyl]OH$ is EtOH ". There is insufficient antecedent basis for this limitation in the claims from which they depend.

Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as well as under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for preparing compounds of formula 1 does not reasonably provide enablement for a dyestuff, antibacterial or herbicidal use.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in scope with these claims. A survey of the specification noted that the specification did not explicitly describe any dyestuff, antibacterial or herbicidal composition or use.

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement

requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 18-23 reciting an intended use do not provide a disclosure sufficient to meet the collective requirements of 35 U.S.C. 112, first paragraph, so as to adequately describe and enable the intended use.

The claims encompass starting materials, intermediates and final products all having the same dyestuff, antibacterial or herbicidal use. The state of the art and level of ordinary skill in the art would not predict the same use for all of these products. Neither is the amount of guidance provided by the specification sufficient to adequately describe and properly enable the claims. there is no disclosure or exemplification in the specification to support dyestuff, antibacterial or herbicidal compositions and uses.

Undue experimentation would be necessary to determine the recited uses. The specification provides no disclosure to support these uses.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, because specification because it does not reasonably provide enablement for the treatment of HIV or AIDS. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention: The nature of the invention is a method for the treatment of HIV or AIDS.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability and no established correlation between in vitro activity and the treatment of viral conditions such as HIV as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary

knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

It is well known in the art that treatment of one mammal with one compound to treat one viral infection does not predict the treatment of another different mammal with a different compound to treat a different viral infection. By using the term treatment of humans, and all mammals, in the claim language, applicants are necessarily extending the treatment and detection to (or compositions) which have not been demonstrated to be effective.

In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would not the nexus between the between in vitro activity and the treatment of viral infections, particularly in vivo, in a particular mammal or human.

Hence, in the absence of a showing of a nexus between any and all known viral infections and the claimed compounds, one of ordinary skill in the art is unable to fully predict possible results from the administration of the claimed compounds.

The presence or absence of working examples: In addition, there is no proof that the claimed compounds or compositions have ever been administered to a human or to an animal model other than mice. The obstacles to therapeutic approaches and detection with regard to viral infections and detection are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to: 1) the extensive genomic diversity, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) the complexity and variation of the elaboration of the disease.

There are insufficient exemplifications to support the treatment of all known viral infections encompassed by claim 17 where only mice and in vitro data are exemplified.

The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. In order to provide proof of utility with regard to

drugs and their uses, either clinical in vivo or in vitro data correlative to in vivo applicability or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established as set forth in full, clear and exact terms in the scope of the disclosure. When the utility is directed to humans, the data must generally be clinical, however, adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept correlation to human utility. Thus, in order to rely on animal data, there must exist an art recognized animal model for testing purposes. In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

The amount of direction or guidance present: There is no proof that the claimed compounds or compositions have ever been administered to a human or to an animal model or than mice.

The breadth of the claims: The claims are drawn to the treatment of any and all for HIV or AIDS.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine which HIV infections out of all such known infections would be benefited by the compounds of claim 1 and then would further need to determine which of the claimed

compounds would provide the treatment. The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which viral infections would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad method recited in applicants' claims. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound in order to practice the claimed invention.

> Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success. It is recommended that the scope of the claims be limited.

Applicants' comments have been noted and considered by are not persuasive of patentability. It is well recognized in the art that HIV has multiple stands and

mutants for which each has its own requirement for inhibition, and activity developed in any one strand cannot automatically be extrapolated to another strand (see CA 117:69322, Richman 1966). In vitro studies, even with good in vitro tissue culture assay for a well known "class" of compounds recognized to be effective in treating HIV would fail to achieve adequate intracellular concentrations due to poor bioavailability, rapid clearance rated, sequestration of antiviral by serum proteins, viral drug resistance (see Oberg and Vrang, Yarchoan et al. or Flexner and Hendrix). Although in vivo animal model may be used when multiple species have been tested, for HIV in vivo efficacy in human, clinical/human data is preferred (Ex parte Balzarini 21 USPQ2nd 1894).

Upon reconsideration the rejections under 35 USC 102 and 103 have been withdrawn as the cited prior art does nor teach or suggest the invention as presently recited in the claims and neither does it provide a reason to modify any reference to obtain the claimed invention.

Claims 14-16 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, C. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond Covington
Examiner
Art Unit 1625

RKC

8/3/05